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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,339	01/03/2006	Barrie Bode	SLU03-010	8839

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EXAMINER	
PITRAK, JENNIFER S	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,339	BODE, BARRIE	
	Examiner	Art Unit	
	JENNIFER PITRAK	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *16,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 17-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/484,728, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Application 60/484,728 does not contain the instantly claimed SEQ ID NO: 3. Therefore, the claims are granted priority to the filing date of the instant application, 06/30/2004.

Election/Restrictions

Claims 16, 26, and 27 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable

generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/20/2007.

Applicant's election with traverse of Group 5, to claims 1-25 and polynucleotide sequence, SEQ ID NO: 3, in the reply filed on 12/20/2007 is acknowledged. The traversal is on the ground(s) that Groups 3-8 or at least Groups 5-8 can be examined without serious burden to the Examiner. This is not found persuasive because each nucleotide sequences of each Group has a distinct structure and requires a distinct search. The requirement is still deemed proper and is therefore made FINAL.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 1-15 and 17-25 are under examination, insofar as they pertain to SEQ ID NO:3.

Claim Objections

Claims 8, 20, 22, and 23 are objected to because of the following informalities: claims 8 and 20 refer to a single independent claim in the plural sense, as "any one of claims 1" (claim 8) and "any one of claims 19 (claim 20). Claims 22 and 23 are duplicate claims. Appropriate correction is required.

Applicant is advised that should claims 11 and 13 be found allowable, claims 12 and 14 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). The phrase, "consisting essentially of" is considered equivalent to "comprising" according to MPEP 2111.03

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 and 6 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Kilberg, *et al.* (1980, JBC, v.255:40119-9) as evidenced by Han, *et al.* (1999, U.S. Patent 5,891,864).

The claims are to a method of inducing apoptosis in a hepatocarcinoma cell by contacting the cell with an agent that inhibits glutamine uptake by modulating a component of a glutamine transport system.

Kilberg, *et al.* teach the inhibition of glutamine uptake in Ehrlich cells, which are hepatocarcinoma cells (see lines 11-14, column 3 of Han, *et al.*), by contacting the cells

with a series of glutamine uptake inhibitors listed in Table IV on p.4014. Thus, Kilberg, *et al.* clearly anticipate the instant claims 1-3 and 6.

Claims 1-3 and 5-8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Bode, *et al.*, (1998, Surgery, v.124:260-8).

The claims are to a method of inducing apoptosis of a hepatocarcinoma cell (including SK-Hep cells) comprising contacting the cell with an agent, wherein the agent inhibits the uptake of glutamine by the cell and the cell undergoes apoptosis, and wherein the agent inhibits ATB0 activity.

Bode, *et al.*, teach treatment of SK-Hep cells with PMA (phorbol 12-myristate 13-acetate) (Figure 6 and p.264, last paragraph). PMA inhibits glutamine transport via ATB0 as taught by Bode, *et al.* at p.262, first paragraph under Results, which reads, "This phorbol ester-induced reduction in System B0-mediated glutamine transport activity was dependent on the concentration of PMA..." Absent evidence to the contrary, treatment of SK-Hep cells with PMA would cause the treated cells to undergo apoptosis, as claimed. Thus, Bode, *et al.*, clearly anticipate each of claims 1-3 and 5-8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bode, *et al.* (1998, Surgery, v.124:260-8, cited by Applicant on p.3, ¶ [0007]).

The claims are to a method of inducing apoptosis of a hepatocarcinoma cell in a patient comprising contacting a cell with an agent that inhibits the uptake of glutamine by the cell.

Bode, *et al.*, teach the inhibition of ATB0 by contacting SK-Hep cells with PMA (described above, in the 35 USC § 102(b) rejection). Bode, *et al.*, do not teach a method wherein the contacted cells are in a patient. However, it would have been obvious to use an agent to contact cells in a patient because at the last sentence on p.266, Bode, *et al.*, suggest the use of ATB0 (transporter) inhibitors in patients by saying "[A]lthough this transporter is also expressed in normal human tissues, the hope is that tumor-specific differences in its regulation can ultimately be exploited in the development of new therapies for HCC." Although Bode, *et al.*, do not specifically teach that inhibition of ATB0 activity induces apoptosis, because the authors teach the step recited in the instant claims, this step is considered to have the effect of inducing apoptosis, absent evidence to the contrary. Thus, claims 1-8 and 24 would have been obvious at the time of the instant application.

Claims 1-15 and 17-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bode, *et al.* as applied to claims 1-8 and 24 above, and further in view of Khvorova, *et al.* (US 2007/0031844, filed as U.S. Provisional Application 60/502,050 on 09/10/2003).

The claims are to methods of treating an hepatocarcinoma and of inducing apoptosis of a hepatocarcinoma cell comprising contacting a cell with an agent that inhibits cellular glutamine uptake by inhibiting ATB0 activity, and wherein the agent is a polynucleotide comprising or consisting essentially of SEQ ID NO: 3 or a vector comprising SEQ ID NO: 3, particularly an adenovirus vector comprising SEQ ID NO: 3. The phrase, "consisting essentially of" is considered equivalent to "comprising" according to MPEP 2111.03, which states "For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, 'consisting essentially of' will be construed as equivalent to 'comprising.' "

Bode, *et al.* teach inhibition of ATB0 activity in cells and in a patient as described above under the 102(b) and 103(a) rejections. Bode, *et al.* does not teach inhibition of ATB0 activity with a polynucleotide or a vector comprising a polynucleotide comprising SEQ ID NO: 3.

Khvorova, *et al.* teach the use of siRNAs for inhibiting gene expression via RNA interference (RNAi). They specifically teach SEQ ID NO: 461989, which is the same as the instant SEQ ID NO: 3 as shown.

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                          SEQ ID NO: 3  5'-aggaggtgctcgattcgtt-3'
                                          ||||||||||||||||||
Khvorova, et al. SEQ ID NO: 461989  5'-aggaggugcucgauucguu-3'
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Khvorova, *et al.* teach that the siRNAs of their invention can be introduced into cells through vectors such as adenovirus vectors (p. 19, ¶ [0277]) and that the siRNAs can be used as therapeutics (*i.*e. in a patient) (p.1, ¶ [0009]).

It would have been obvious to perform the method of inhibiting ATB0 activity in a hepatocarcinoma cell as taught by Bode, *et al.*, with the nucleotide SEQ ID NO: 3 because Khvorova, *et al.* teach the use of SEQ ID NO: 461989 or a vector comprising SEQ ID NO: 461989 to inhibit gene (ATB0) expression in cells and in a patient (therapy). One would reasonably expect success in using the nucleotide for ATB0 gene inhibition because Khvorova, *et al.* teach that the siRNAs of their invention are useful as therapeutic agents against disease. Thus, claims 1-15 and 17-25 would have been obvious to one skilled in the art at the time of the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JENNIFER PITRAK whose telephone number is (571)270-3061. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jennifer Pitrak, PhD
Examiner
Art Unit 1635

/Tracy Vivlemore/
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